Study of Attention Deficit Hyperactivity Symptoms in Children with Rheumatic History

Thesis

Submitted for Partial Fulfilment of Master Degree in Pediatrics

By

Rania Mohey El-Din Ahmed

M.B,Bch. 2003

Ain Shams University

Under supervision of

Prof.Dr. Mohammed Mohammed Farid

Professor of Pediatrics

Faculty of Medicine – Ain Shams University

Dr. Ola Abd Elaziz Elmasry

Assistant Professor of Pediatrics

Faculty of Medicine – Ain Shams University

Dr. Azza Mohammed Youssef

Lecturer of Pediatrics

Faculty of Medicine – Ain Shams University

Faculty of Medicine

Ain Shams University

2010

ACKNOWLEDGEMENT

First and foremost thanks **GOD** for fulfillment of this work.

I would like to express my sincere gratitude to **PROFESSOR DR. MOHAMMED MOHAMMED FARID**, Professor of Pediatrics, Faculty of Medicine, Ain Shams University, who honored me by his great support and his kind supervision. It is really great to work under his guidance.

Moreover, I am greatly indebted to **DR.OLA MOHAMMED ELMASRY,** Assistant Professor of Pediatrics, Faculty of Medicine, Ain Shams University, for her continuous encouragement, support and giving a great deal of her valuable time in revising every item in this work.

Furthurmore, I wish to express my deepest thanks to **DR. AZZA YOUSSEF**, lecturer of Pediatrics, Faculty of Medicine, Ain Shams University, who was very helpful in managing this work and for her keen perception, continuous help, support, and meticulous guidance throughout this work.

Rania Mohey El-Din Ahmed

دراسة أعراض فرط الحركة و قلة التركيز لدى الاطفال ذو تاريخ مرضى للحمى الروماتزمية

رسالة

مقدمة من

الطبيبة/ رانيا محى الدين احمد

بكالوريوس الطب والجراحة العامة- ٢٠٠٣

جامعة عين شمس

توطئة للحصول على ماجستير فى طب الاطفال

تحت اشراف

أ.د/ محمد محمد فريد

أستاذ طب الاطفال

كلية الطب - جامعةعين شمس

د/علا عبد العزيز المصرى

أستاذ مساعد طب الاطفال

كلية الطب - جامعةعين شمس

د/عزة محمد يوسف

مدرس طب الاطفال

كلية الطب - جامعةعين شمس

كلية الطب

جامعة عين شمس

٢٠١٠

CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

ARF	Acute rheumatic fever
ASOT	Antistreptolysin O Titre
ADHD	Attention deficit hyperactivity
BID	twice per day
CD	Conduct disorder
CHF	Congestive heart failure
CNS	Central nervous system
CRP	C-reactive protein
CTPRS–R	Conner's Parent Rating Scale-Revised
CXR	Chest X - ray
DSM-IV-R	The Diagnostic and Statistical Manual of Mental Disorders, fourth edition, revised
ECG	Electrocardiogram
ESR	Erythrocyte sedimentation rate
GABHS	Group A beta hemolytic streptococcal
GAS	Group A streptococcal
GRTH	Generalized resistance to thyroid hormone
HIV	Human immunodeficiency virus
IM	Intramuscular
IQR	Interquartile range
IV	Intravenous
IVIG	Intravenous immunoglobulin
NBTE	Non bacterial thrombotic endocarditis
NIMH	Institute of Mental Health
OCD	Obsessive compulsive disorder
ODD	Oppositional Defiant Disorder
PANDAS	Pediatric autoimmune neuropsychiatric disorder associated with streptococcal infection
RA	Rheumatoid arthritis
RF	Rheumatic fever
RHD	Rheumatic heart disease

INTRODUCTION

Rheumatic fever is an inflammatory disease that may develop after an infection with Streptococcus bacteria (such as streptococcal sore throat or scarlet fever). The disease can affect the heart, joints, skin, and brain.

Rheumatic fever mainly affects children ages 6 -15yrs, and occurs approximately 20 days after streptococcal sore throat or scarlet fever.

Sydenham's chorea is a major manifestation of acute rheumatic fever and is the only evidence of Rheumatic fever in approximately 20% of cases ***(Kliegman et al., 2007).***

Sydenham's chorea is the most common form of autoimmune chorea. Despite the decline in its frequency worldwide, it remains the most prevalent form of chorea in children even in developed areas. Its usual age of onset is 8 to 9 years, but some patients have developed chorea during the third decade of life.

In most series, there is a female preponderance. Typically, patients develop Sydenham's chorea 4 to 8 weeks after an episode of group A beta haemolytic streptococcal pharyngitis. It is estimated that no more than one quarter of patients with acute Rheumatic fever develop Sydenham's chorea ***(Cardoso 2006).***

Sydenham's chorea is characterized by motor: mainly choreic involuntary movements and psychiatric symptoms: including anxiety, depression, obsessive compulsive, attention deficit hyperactivity disorders. Symptoms of Sydenham's chorea may be considered as result of basal ganglia dysfunction determined by autoimmune mechanisms elicited by streptococcal infection ***(Teixeira et al., 2007).***

Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infection (PANDAS) shares the same mechanism with Sydenham's chorea, but (PANDAS) has not been shown to require penicillin prophylaxis. Thus it is important to distinguish between them ***(Gimzal et al., 2002).***

Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental condition where the affected children have inattention, impulsiveness and hyperactivity. The Diagnostic and Statistical Manual of Mental Disorders: Fourth Edition (DSM-IV) requires the presence of at least six out of nine behavioural features that must have been present for at least six months, are present in all settings to diagnose ADHD. ADHD had onset before the age of seven and are causing significant distress or impairment ***(Carter et al., 2008).***

Attention deficit hyperactivity symptoms have been described in patients with Sydenham's chorea ***(Gimzal et al., 2002).***

AIM OF THE WORK

This study will examine the frequency of occurrence, age at onset and description of attention deficit hyperactivity symptoms among children with history of Rheumatic fever with or without Sydenham's chorea.

CHAPTER 1

RHEUMATIC FEVER

Rheumatic fever (RF) is an inflammatory disease that may develop after an infection with streptococcus bacteria (such as streptococcal sore throat, scarlet fever). The disease can affect the heart, joints, skin, and brain. Rheumatic fever is common worldwide and is responsible for many cases of damaged heart valves. Rheumatic fever mainly affects children ages 5-15yrs and occurs approximately 20 days after streptococcal sore throat or scarlet fever. Rheumatic Heart Disease (RHD) is a condition in which permanent damage to heart valves is caused by Rheumatic Fever. The heart valve is damaged by a disease process that generally begins with a streptococcal sore throat caused by bacteria called streptococcus, and may eventually cause RF ***(Gerber, 2007).***

RHD is the most serious complication of RF. RHD may develop with varying degrees of Pancarditis with associated valve insufficiency, heart failure, pericarditis and even death. With chronic RHD, patients develop valve stenosis with varying degrees of regurgitation, atrial dilation, arrhythmias, ventricular dysfunction ***(*Bandaru *et al., 2009).***

Incidence

Rheumatic Heart Disease continues to be a common health problem in the developing world, causing morbidity and mortality

among the children and adults. Recent reports from the developing world have documented Rheumatic Fever (RF) incidence rates as high as 206/100,000 and RHD prevalence rates as high as 18.6/1000. The high frequency of RHD in developing world necessitates aggressive prevention and control measures ***(Alkhalifa et al., 2008).***

Pathophysiology

Rheumatic fever is a systemic disease affecting the peri-arteriolar connective tissue and can occur after an untreated Group A Beta hemolytic streptococcal pharyngeal infection. It is believed to be caused by antibody cross-reactivity. This cross-reactivity is Type II hypersensitivity reaction and is termed molecular mimicry usually; self reactive B cells remain anergic in the periphery without T cell co-stimulation. During a Streptococcal infection, activated antigen presenting cells such as macrophages present the bacterial antigen to helper T cells. Helper T cells subsequently activate B cells and induce the production of antibodies against the cell wall of Streptococcus. However the antibodies may also react against the myocardium and joints, producing the symptoms of rheumatic fever ***(Abbas et al., 2004).***

Group A streptococcus pyogenes has a cell wall composed of branched polymers which sometimes contain "M proteins" that are highly antigenic .The antibodies which the immune system generates against the "M proteins" may cross react with cardiac myofiber protein myosin and smooth muscle cells of arteries,

inducing cytokines release and tissue destruction ***(Fae et al., 2006).***

In acute RF, the lesions can be found in any layer of the heart and hence it called pancarditis. The inflammation may cause a serofibrinous pericardial exudates described as “bread-and-butter” pericarditis, which usually resolves without sequelae ***(Cotran et al., 2005).***

Chronic rheumatic heart disease is characterized by repeated inflammation with fibrinous resolution. The cardinal anatomic changes of the valve include leaflet thickening, commissural fusion, shortening and thickening of the tendinous cords ***(Cotran et al., 2005).***

Clinical features

ARF typically lags behind streptococcal pharyngitis by 2 to 3 weeks. As a result, isolating GAS infection from the oropharynx at disease onset is rare. The peak onset is at age 6 to 20 years. About 70% of older children and young adults can recall an episode of pharyngitis, only 20% of younger children recollect having a sore throat. The disease onset most often is characterized by an acute febrile illness accompanied by a large-joint migratory arthritis, possibly with concomitant signs of carditis and valvular inflammation or with CNS involvement and chorea. Although acute episodes typically are self-limited, they may lead to chronic progressive heart disease and cardiac decompensation ***(Golbus et al., 2009).***

1-Arthritis

This is the most common symptom of ARF and often the first one to appear, especially in teenagers and young adults. The arthritis typically is a migratory, nondeforming, large-joint polyarthritis, especially of the knees, ankles, elbows, and wrists. If the arthritis goes unmanaged, several joints are affected in quick succession, with each joint inflamed maximally for a few days to a week. The inflammation then decreases over the course of the week before disappearing, it typically lasts no longer than 4 weeks ***(Chin, 2009).***

The pain associated with this migratory arthritis often is much more pronounced than the objective signs of disease. Physicians often manage the arthritis and arthralgia of ARF symptomatically early in their course. However, doing so may change the clinical presentation and deprive clinicians of seeing the characteristic signs of ARF. Involvement of a single large joint was common (25% of cases); the knee and ankle joints were affected most often. Less frequently affected were the elbow, wrist, hip joints and the small joints of the feet (12% to 15% of cases) ***(Chin, 2009)***.

2-Carditis

Cardiac involvement in ARF may include valvulitis, myocarditis and pericarditis. Isolated mitral valve disease develops in nearly 60% of patients with carditis; combined mitral and aortic valve involvement is the next most common **(Figure 1)**.